

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

APPLICATION NO.: 09/672,126

PRIORITY DOCKET NO.: C1039/7044

FILING DATE: September 27, 2000

APPLICANT: Hartmann et al.

GROUP ART UNIT: 1646

EXAMINER: unknown

Sheet 1 of 5

JUN 14 2001

PATENT &amp; TRADEMARK OFFICE

## U.S. PATENT DOCUMENTS

Examiner's Initials#	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
QW	A15	6,194,388	B1	Krieg et al.	02-27-2001
	A16	6,207,646	B1	Krieg et al.	03-27-2001
	A17	6,214,804	B1	Felgner et al.	04-10-2001
	A18	6,214,806	B1	Krieg et al.	04-10-2001
	A19	6,218,371	B1	Krieg et al.	04-17-2001
QW	A20	6,239,116	B1	Krieg et al.	05-29-2001

## FOREIGN PATENT DOCUMENTS

Examiner's Initials#	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/Country	Number	Kind Code			
QW	B20	EPO	0 855 184	A1		07-29-1998	
	B21	WIPO	WO98/32462	A1		07-30-1998	
	B22	WIPO	WO98/33517	A1		08-06-1998	
	B23	WIPO	WO98/55495	A2		10-12-1998	
	B24	WIPO	WO99/51259	A2		10-14-1999	
	B25	WIPO	WO99/56755	A1		11-11-1999	
	B26	WIPO	WO99/58118	A2		11-18-1999	
	B27	WIPO	WO99/61056	A2		12-02-1999	
	B28	WIPO	WO00/06588	A1		02-10-2000	
	B29	WIPO	WO00/14217	A3		03-16-2000	
	B30	WIPO	WO00/67023	A1		11-09-2000	
QW	B31	WIPO	WO01/22972	A1		04-05-2001	

## OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials#	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)	
QW	C66	AZAD RF et al., Antiviral activity of a phosphorothioate oligonucleotide complementary to RNA of the human cytomegalovirus major immediate-early region. <i>Antimicrob Agents Chemother.</i> 1993 Sep;37(9):1945-54.		
	C67	AZUMA I, Biochemical and immunological studies on cellular components of tubercle bacilli. <i>Kekkaku</i> 1992;67(9):45-55.		
	C68	BARTHOLOME EJ et al., Interferon-beta induce the maturation of IL-12-deficient myeloid dendritic cells able to induce Th2 type cytokine secretion. <i>J Interferon Cytokine Res.</i> 1999;19(Suppl 1):S81.		
	C69	BAYEVER E et al., Systemic administration of a phosphorothioate oligonucleotide with a sequence complementary to p53 for acute myelogenous leukemia and myelodysplastic syndrome: initial results of a phase I trial. <i>Antisense Res Dev.</i> 1993 Winter;3(4):383-90.		
	C70	BENNETT RM et al., DNA binding to human leukocytes. Evidence for a receptor-mediated association, internalization, and degradation of DNA. <i>J Clin Invest.</i> 1985 Dec;76(6):2182-90.		
	C71	BLAXTER ML et al., Genes expressed in <i>Brugia malayi</i> infective third stage larvae. <i>Mol Biochem Parasitol.</i> 1996 Apr;77(1):77-93.		
QW	C72	BOGGS RT et al., Characterization and modulation of immune stimulation by modified oligonucleotides. <i>Antisense Nucleic Acid Drug Dev.</i> 1997 Oct;7(5):461-71.		

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

APPLICATION NO.: 09/672,126

FY. DOCKET NO.: C1039/7044

FILING DATE: September 27, 2000

APPLICANT: Hartmann et al.

GROUP ART UNIT: 1646

EXAMINER: unknown

Sheet 2

JUN 1 4 2001

PATENT TRADEMARK OFFICE

QW	C73	BRANDARF et al., Amplification of antibody production by phosphorothioate oligodeoxynucleotides. <i>J Lab Clin Med.</i> 1996 Sep;128(3):329-38.		
	C74	BRANDA RF et al., Immune stimulation by an antisense oligomer complementary to the rev gene of HIV-1. <i>Biochem Pharmacol.</i> 1993 May 25;45(10):2037-43.		
	C75	CELLA M et al., Maturation, activation, and protection of dendritic cells induced by double-stranded RNA. <i>J Exp Med.</i> 1999 Mar 1;189(5):821-9.		
	C76	CHACE JH et al., Regulation of differentiation in CD5+ and conventional B cells. Sensitivity to LPS-induced differentiation and interferon-gamma-mediated inhibition of differentiation. <i>Clin Immunol Immunopathol.</i> 1993 Sep;68(3):327-32.		
	C77	CHANG YN et al., The palindromic series I repeats in the simian cytomegalovirus major immediate-early promoter behave as both strong basal enhancers and cyclic AMP response elements. <i>J Virol.</i> 1990 Jan;64(1):264-77.		
	C78	CHU RS et al., CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. <i>J Exp Med.</i> 1997 Nov 17;186(10):1623-31.		
	C79	CRYSTAL RG, Transfer of genes to humans: early lessons and obstacles to success. <i>Science.</i> 1995 Oct 20;270(5235):404-10.		
	C80	ENGLISCH U et al., Chemically modified oligonucleotides as probes and inhibitors. <i>Angew Chemie Int Ed Engl.</i> 1991 Jun;30(6):613-29.		
	C81	ERB KJ et al., Infection of mice with Mycobacterium bovis-Bacillus Calmette-Guerin (BCG) suppresses allergen-induced airway eosinophilia. <i>J Exp Med.</i> 1998 Feb 16;187(4):561-9.		
	C82	ETLINGER HM, Carrier sequence selection--one key to successful vaccines. <i>Immunol Today.</i> 1992 Feb;13(2):52-5.		
	C83	FERBAS JJ et al., CD4+ blood dendritic cells are potent producers of IFN-alpha in response to in vitro HIV-1 infection. <i>J Immunol.</i> 1994 May 1;152(9):4649-62.		
	C84	GURA T, Antisense has growing pains. <i>Science.</i> 1995 Oct 27;270(5236):575-7.		
	C85	HADDEN JW et al., Immunopharmacology. Immunomodulation and immunotherapy. <i>JAMA.</i> 1992 Nov 25;268(20):2964-9.		
	C86	HADDEN JW, Immunostimulants. <i>Trends Pharmacol Sci.</i> 1993 May;14(5):169-74.		
	C87	HATZFELD J et al., Release of early human hematopoietic progenitors from quiescence by antisense transforming growth factor beta 1 or Rb oligonucleotides. <i>J Exp Med.</i> 1991 Oct 1;174(4):925-9.		
	C88	HIGHFIELD PE, Sepsis: the more, the murkier. <i>Biotechnology (NY).</i> 1994 Aug;12(8):828.		
	C89	IGUCHI-ARIGA SM et al., CpG methylation of the cAMP-responsive enhancer/promoter sequence TGACGTCA abolishes specific factor binding as well as transcriptional activation. <i>Genes Dev.</i> 1989 May;3(5):612-9.		
	C90	ISHIKAWA R et al., IFN induction and associated changes in splenic leukocyte distribution. <i>J Immunol.</i> 1993 May 1;150(9):3713-27.		
	C91	IVERSEN PL et al., Pharmacokinetics of an antisense phosphorothioate oligodeoxynucleotide against rev from human immunodeficiency virus type 1 in the adult male rat following single injections and continuous infusion. <i>Antisense Res Dev.</i> 1994 Spring;4(1):43-52.		
	C92	JAKWAY JP et al., Growth regulation of the B lymphoma cell line WEHI-231 by anti-immunoglobulin, lipopolysaccharide, and other bacterial products. <i>J Immunol.</i> 1986 Oct 1;137(7):2225-31.		
	C93	JAROSZEWSKI JW et al., Cellular uptake of antisense oligodeoxynucleotides. <i>Adv Drug Del Rev</i> 1991;6(3):235-50.		
	C94	KATAOKA T et al., Antitumor activity of synthetic oligonucleotides with sequences from cDNA encoding proteins of Mycobacterium bovis BCG. <i>Jpn J Cancer Res.</i> 1992 Mar;83(3):244-7.		
	C95	KLINMAN DM et al., Contribution of CpG motifs to the immunogenicity of DNA vaccines. <i>J Immunol.</i> 1997 Apr 15;158(8):3635-9.		
QW	C96	KRIEG AM et al., A role for endogenous retroviral sequences in the regulation of lymphocyte activation. <i>J Immunol.</i> 1989 Oct 15;143(8):2448-51.		

FORM PTO-1449/A and B (Modified)		APPLICATION NO.: 09/672,126	...TY. DOCKET NO.: C1039/7044
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		FILING DATE: September 27, 2000	
		APPLICANT: Hartmann et al.	
		GROUP ART UNIT: 1646	EXAMINER: unknown
Sheet	3	of	5

JUN 14 2001  
PATENT & TRADEMARK OFFICE

QW	C97	KRIEG AM et al., Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholesteryl moiety increases cellular association and improves efficacy. <i>Proc Natl Acad Sci U S A</i> . 1993 Feb 1;90(3):1048-52.		
	C98	KRIEG AM et al., Oligodeoxynucleotide modifications determine the magnitude of B cell stimulation by CpG motifs. <i>Antisense Nucleic Acid Drug Dev</i> . 1996 Summer;6(2):133-9.		
	C99	KRIEG AM et al., Phosphorothioate oligodeoxynucleotides: antisense or anti-protein? <i>Antisense Res Dev</i> . 1995 Winter;5(4):241.		
	C100	KRIEG AM et al., The role of CpG dinucleotides in DNA vaccines. <i>Trends Microbiol</i> . 1998 Jan;6(1):23-7.		
	C101	KRIEG AM et al., Uptake of oligodeoxyribonucleotides by lymphoid cells is heterogeneous and inducible. <i>Antisense Res Dev</i> . 1991 Summer;1(2):161-71.		
	C102	KRIEG AM, An innate immune defense mechanism based on the recognition of CpG motifs in microbial DNA. <i>J Lab Clin Med</i> . 1996 Aug;128(2):128-33.		
	C103	KRIEG AM, CpG DNA: a pathogenic factor in systemic lupus erythematosus? <i>J Clin Immunol</i> . 1995 Nov;15(6):284-92.		
	C104	KRIEG AM, Leukocyte stimulation by oligodeoxynucleotides. In: <i>Applied Antisense Oligonucleotide Technology</i> , Stein CA and Krieg AM, eds., New York: Wiley-Liss, 1998; pp.431-438.		
	C105	KURAMOTO E et al., Oligonucleotide sequences required for natural killer cell activation. <i>Jpn J Cancer Res</i> . 1992 Nov;83(11):1128-31.		
	C106	LIPFORD GB et al., Bacterial DNA as immune cell activator. <i>Trends Microbiol</i> . 1998 Dec;6(12):496-500.		
	C107	LIPFORD GB et al., CpG-containing synthetic oligonucleotides promote B and cytotoxic T cell responses to protein antigen: a new class of vaccine adjuvants. <i>Eur J Immunol</i> . 1997 Sep;27(9):2340-4.		
	C108	LIPFORD GB et al., Immunostimulatory DNA: sequence-dependent production of potentially harmful or useful cytokines. <i>Eur J Immunol</i> . 1997 Dec;27(12):3420-6.		
	C109	MACFARLANE DE et al., Antagonism of immunostimulatory CpG-oligodeoxynucleotides by quinacrine, chloroquine, and structurally related compounds. <i>J Immunol</i> . 1998 Feb 1;160(3):1122-31.		
	C110	MANZEL L et al., CpG-oligodeoxynucleotide-resistant variant of WEHI 231 cells. <i>J Leukoc Biol</i> . 1999 Nov;66(5):817-21.		
	C111	MASTRANGELO MJ et al., Gene therapy for human cancer: an essay for clinicians. <i>Semin Oncol</i> . 1996 Feb;23(1):4-21.		
	C112	MATSON S et al., Nonspecific suppression of [3H]thymidine incorporation by "control" oligonucleotides. <i>Antisense Res Dev</i> . 1992 Winter;2(4):325-30.		
	C113	McINTYRE KW et al., A sense phosphorothioate oligonucleotide directed to the initiation codon of transcription factor NF-kappa B p65 causes sequence-specific immune stimulation. <i>Antisense Res Dev</i> . 1993 Winter;3(4):309-22.		
	C114	MESSINA JP et al., Stimulation of in vitro murine lymphocyte proliferation by bacterial DNA. <i>J Immunol</i> . 1991 Sep 15;147(6):1759-64.		
	C115	MESSINA JP et al., The influence of DNA structure on the in vitro stimulation of murine lymphocytes by natural and synthetic polynucleotide antigens. <i>Cell Immunol</i> . 1993 Mar;147(1):148-57.		
	C116	MOJCIK CF et al., Administration of a phosphorothioate oligonucleotide antisense to murine endogenous retroviral MCF env causes immune effects in vivo in a sequence-specific manner. <i>Clin Immunol Immunopathol</i> . 1993 May;67(2):130-6.		
	C117	MOTTRAM JC et al., A novel CDC2-related protein kinase from <i>Leishmania mexicana</i> , LmmCRK1, is post-translationally regulated during the life cycle. <i>J Biol Chem</i> . 1993 Oct 5;268(28):21044-52.		
	C118	NYCE JW et al., DNA antisense therapy for asthma in an animal model. <i>Nature</i> . 1997 Feb 20;385(6618):721-5.		
GW	C119	PISETSKY DS et al., Stimulation of murine lymphocyte proliferation by a phosphorothioate oligonucleotide with antisense activity for herpes simplex virus. <i>Life Sci</i> . 1994;54(2):101-7.		

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

FILING DATE: September 27, 2000

APPLICANT: Hartmann et al.

GROUP ART UNIT: 1646

EXAMINER: unknown

Sheet 4 5

PATENT & TRADEMARK OFFICE  
JUN 14 2001

Q1	C120	PISETSKY DS et al., The influence of base sequence on the immunological properties of defined oligonucleotides. <i>Immunopharmacology</i> . 1998 Nov;40(3):199-208.		
	C121	PISETSKY DS, Immunologic consequences of nucleic acid therapy. <i>Antisense Res Dev</i> . 1995 Fall;5(3):219-25.		
	C122	PISETSKY DS, The immunologic properties of DNA. <i>J Immunol</i> . 1996 Jan 15;156(2):421-3.		
	C123	RAZ E et al., Preferential induction of a Th1 immune response and inhibition of specific IgE antibody formation by plasmid DNA immunization. <i>Proc Natl Acad Sci U S A</i> . 1996 May 14;93(10):5141-5.		
	C124	ROMAN M et al., Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. <i>Nat Med</i> . 1997 Aug;3(8):849-54.		
	C125	SCHNELL N et al., Identification and characterization of a <i>Saccharomyces cerevisiae</i> gene (PAR1) conferring resistance to iron chelators. <i>Eur J Biochem</i> . 1991 Sep 1;200(2):487-93.		
	C126	SHIRAKAWA T et al., The inverse association between tuberculin responses and atopic disorder. <i>Science</i> . 1997 Jan 3;275(5296):77-9.		
	C127	SPARWASSER T et al., Macrophages sense pathogens via DNA motifs: induction of tumor necrosis factor-alpha-mediated shock. <i>Eur J Immunol</i> . 1997 Jul;27(7):1671-9.		
	C128	STEIN CA et al., Oligodeoxynucleotides as inhibitors of gene expression: a review. <i>Cancer Res</i> . 1988 May 15;48(10):2659-68.		
	C129	STULL RA et al., Antigene, ribozyme and aptamer nucleic acid drugs: progress and prospects. <i>Pharm Res</i> . 1995 Apr;12(4):465-83.		
	C130	SUBRAMANIAN PS et al., Theoretical considerations on the "spine of hydration" in the minor groove of d(CGCGAATTCGCG).d(GCGCTTAAGCGC): Monte Carlo computer simulation. <i>Proc Natl Acad Sci U S A</i> . 1988 Mar;85(6):1836-40.		
	C131	TANAKA T et al., An antisense oligonucleotide complementary to a sequence in I gamma 2b increases gamma 2b germline transcripts, stimulates B cell DNA synthesis, and inhibits immunoglobulin secretion. <i>J Exp Med</i> . 1992 Feb 1;175(2):597-607.		
	C132	VALLIN H et al., Anti-double-stranded DNA antibodies and immunostimulatory plasmid DNA in combination mimic the endogenous IFN-alpha inducer in systemic lupus erythematosus. <i>J Immunol</i> . 1999 Dec 1;163(11):6306-13.		
	C133	WAGNER RW, Gene inhibition using antisense oligodeoxynucleotides. <i>Nature</i> . 1994 Nov 24;372(6504):333-5.		
	C134	WALLACE RB et al., Oligonucleotide probes for the screening of recombinant DNA libraries. <i>Methods Enzymol</i> . 1987;152:432-42.		
	C135	WU GY et al., Receptor-mediated gene delivery and expression in vivo. <i>J Biol Chem</i> . 1988 Oct 15;263(29):14621-4.		
	C136	WU-PONG S, Oligonucleotides: opportunities for drug therapy and research. <i>Pharm Technol</i> . 1994 Oct;18:102-14.		
	C137	YAMAMOTO S et al., Mode of action of oligonucleotide fraction extracted from <i>Mycobacterium bovis</i> BCG. <i>Kekkaku</i> 1994;69(9):29-32.		
	C138	YAMAMOTO T et al., Lipofection of synthetic oligodeoxyribonucleotide having a palindromic sequence of AACGTT to murine splenocytes enhances interferon production and natural killer activity. <i>Microbiol Immunol</i> . 1994;38(10):831-6.		
	C139	YAMAMOTO T et al., Synthetic oligonucleotides with certain palindromes stimulate interferon production of human peripheral blood lymphocytes in vitro. <i>Jpn J Cancer Res</i> . 1994 Aug;85(8):775-9.		
	C140	YI AK et al., IFN-gamma promotes IL-6 and IgM secretion in response to CpG motifs in bacterial DNA and oligodeoxynucleotides. <i>J Immunol</i> . 1996 Jan 15;156(2):558-64.		
	C141	ZHAO Q et al., Comparison of cellular binding and uptake of antisense phosphodiester, phosphorothioate, and mixed phosphorothioate and methylphosphonate oligonucleotides. <i>Antisense Res Dev</i> . 1993 Spring;3(1):53-66.		
Q2	C142	ZHAO Q et al., Stage-specific oligonucleotide uptake in murine bone marrow B-cell precursors. <i>Blood</i> . 1994 Dec 1;84(11):3660-6.		

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

APPLICATION NO.: 09/672,126

FY. DOCKET NO.: C1039/7044

FILING DATE: September 27, 2000

APPLICANT: Hartmann et al.

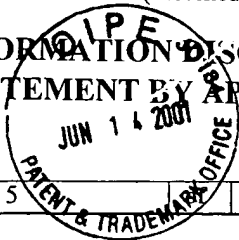
GROUP ART UNIT: 1646

EXAMINER: unknown

Sheet

5

5



EXAMINER

DATE CONSIDERED

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*A copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

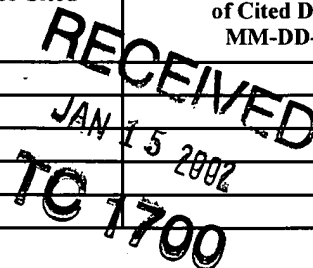
[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]

FORM PTO-1449/A and B (Modified)		APPLICATION NO.: 09/672,126	ATTY. DOCKET NO.: C1039/7044
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		FILING DATE: September 27, 2000	<b>RECEIVED</b> JAN 17 2001 TECH CENTER 1600/2900
		APPLICANT: Hartmann et al.	
		GROUP ART UNIT: 1646	
Sheet 1 of 1	EXAMINER: unknown		



### U.S. PATENT DOCUMENTS

Examiner's Initials#	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		



### FOREIGN PATENT DOCUMENTS

Examiner's Initials#	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/Country	Number	Kind Code			

### OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials#	Cite No.	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
QN	C143	MARTIN J et al., Effects of the ribavirin-interferon alpha combination on cultured peripheral blood mononuclear cells from chronic hepatitis C patients. <i>Cytokine</i> . 1998 Aug;10(8):635-44.	
QN	C144	TAM RC et al., Ribavirin polarizes human T cell responses towards a Type 1 cytokine profile. <i>J Hepatol</i> . 1999 Mar;30(3):376-82.	
QN	C145	TAM RC et al., The ribavirin analog ICN 17261 demonstrates reduced toxicity and antiviral effects with retention of both immunomodulatory activity and reduction of hepatitis-induced serum alanine aminotransferase levels. <i>Antimicrob Agents Chemother</i> . 2000 May;44(5):1276-83.	

EXAMINER <i>Quyn Nguyen</i>	DATE CONSIDERED 8/23/02
--------------------------------	----------------------------

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

[NOTE - Must provide a copy of any patent, publication, other information listed, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]